SEQUENCE LISTING

<110> Genzyme Corporation
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Parsons, Geoffrey

<120> Methods of Treating Diabetes and Other Blood Sugar Disorders

<130> 5062CIP

<140> US 10/716,326
<141> 2003-11-17

<150> US 10/215,272
<151> 2002-08-07

<150> US 60/310,982
<151> 2001-08-08

<160> 54

<170> PatentIn version 3.2

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tgggccacgg cgagggcacc ttcaccagcg acgtgagcag ctacctggag ggccaggccg 120

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<210> 2
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Gly His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu
20 25 30

Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
35 40 45

<210> 3
<211> 250

<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleotide sequence of Exendin-4.GLP-1Gly8

<400> 3
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ccagctccga gagcttcgcc aagcgcatca agcgccacgg cgagggcacc ttcaccagcg 180

acgtgagcag ctacctggag ggccaggccg ccaaggagtt catcgcctgg ctggtgaagg 240

gccgcggctg 250

<210> 4
<211> 78
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence of Exendin-4.GLP-1Gly8

<400> 4

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1 5 10 15

Leu Phe Pro Ile Ser Trp Gln Met Pro Val Glu Ser Gly Leu Ser Ser
20 25 30

Glu Asp Ser Ala Ser Ser Glu Ser Phe Ala Lys Arg Ile Lys Arg His
35 40 45

Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln
50 55 60

Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
65 70 75

<210> 5
<211> 245
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleotide sequence of Helodermin.GLP-1Gly8

<400> 5
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ccctgttccc tgtgagctgg cagatggcca tcaagagcag actgtcctct gaggactctg 120

agacagacca gagactgaag cgcatcaagc gccacggcga gggcaccttc accagcgacg 180

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gcggc 245

<210> 6
<211> 77
<212> PRT
<213> Amino acid sequence of Helodermin.GLP-1Gly8

<400> 6

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1 5 10 15

Leu Phe Pro Val Ser Trp Gln Met Ala Ile Lys Ser Arg Leu Ser Ser
20 25 30

Glu Asp Ser Glu Thr Asp Gln Arg Leu Lys Arg Ile Lys Arg His Gly
35 40 45

Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala
50 55 60

Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
65 70 75

<210> 7
<211> 260
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<223> Nucleotide sequence of GIP.GLP-1Gly8

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tgggcagcca tgccaaggtg agctccccac agaagcgcat caagcgccac ggcgagggca 180

ccttcaccag cgacgtgagc agctacctgg agggccaggc cgccaaggag ttcatcgcct 240

ggctggtgaa gggccgcggc 260

<210> 8
<211> 82
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence of GIP.GLP-1Gly8

<400> 8

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1 5 10 15

Ala Val Gly Leu Gly Glu Lys Lys Glu Gly His Phe Ser Ala Leu Pro

20 25 30

Ser Leu Pro Val Gly Ser His Ala Lys Val Ser Ser Pro Gln Lys Arg
35 40 45

Ile Lys Arg His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
50 55 60

Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
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Arg Gly

<210> 9
<211> 266
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleotide sequence of IGF-1 (furin).GLP-1Gly8

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ccctgtgcct gctgaccttc accagctccg ccacagccaa gcgcatcaag cgccacggcg 180

agggcacctt caccagcgac gtgagcagct acctggaggg ccaggccgcc aaggagttca 240

tcgcctggct ggtgaagggc cgcggc 266

<210> 10
<211> 84
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino sequence of IGF-1 (furin).GLP-1Gly8

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1 5 10 15

Cys Asp Phe Leu Lys Val Lys Met His Thr Met Ser Ser Ser His Leu
20 25 30

Phe Tyr Leu Ala Leu Cys Leu Leu Thr Phe Thr Ser Ser Ala Thr Ala
35 40 45

Lys Arg Ile Lys Arg His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser
50 55 60

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Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val
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Lys Gly Arg Gly
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<220>
<223> Nucleotide sequence of IGF-1.GLP-1Gly8

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tttgtgactt cctgaaggtg aagatgcaca ccatgagctc cagccacctg ttctacctgg 120

ccctgtgcct gctgaccttc accagctccg ccacagccca cggcgagggc accttcacca 180

gcgacgtgag cagctacctg gagggccagg ccgccaagga gttcatcgcc tggctggtga 240

agggccgcgg c 251

<210> 12
<211> 79
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence of IGF-1.GLP-1Gly8

<400> 12

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Cys Asp Phe Leu Lys Val Lys Met His Thr Met Ser Ser Ser His Leu
            20                  25                  30

Phe Tyr Leu Ala Leu Cys Leu Leu Thr Phe Thr Ser Ser Ala Thr Ala
        35                  40                  45

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
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Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
65                  70                  75
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<210> 13
<211> 167
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleotide sequence of Preproglucagon.GLP-1Gly8

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aaggcagctg gcaacacggc gagggcacct tcaccagcga cgtgagcagc tacctggagg 120

gccaggccgc caaggagttc atcgcctggc tggtgaaggg ccgcggc 167

<210> 14
<211> 51
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence of Preproglucagon.GLP-1Gly8

<400> 14

Met Lys Ser Ile Tyr Phe Val Ala Gly Leu Phe Val Met Leu Val Gln
1 5 10 15

Gly Ser Trp Gln His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser
20 25 30

Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys
35 40 45

Gly Arg Gly
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<210> 15
<211> 179
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleotide sequence of Alpha-1 antitrypsin.GLP-1Gly8

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gctgcctggt ccctgtctcc ctggctcacg gcgagggcac cttcaccagc gacgtgagca 120

gctacctgga gggccaggcc gccaaggagt tcatcgcctg gctggtgaag ggccgcggc 179

<210> 16
<211> 55
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence of Alpha-1 antitrypsin.GLP-1Gly8

<400> 16

Met Pro Ser Ser Val Ser Trp Gly Ile Leu Leu Leu Ala Gly Leu Cys
1 5 10 15

Cys Leu Val Pro Val Ser Leu Ala His Gly Glu Gly Thr Phe Thr Ser
20 25 30

Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala
35 40 45

Trp Leu Val Lys Gly Arg Gly
50 55

<210> 17
<211> 245
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleotide sequence of Factor IX.GLP-1Gly8

<400> 17
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ccatctgcct cctgggatac ctcctgtctg ctgagtgcac agtgttcctg gaccatgaga 120

atgccaacaa gattctgaac agacccaaga ggcatgggga gggcaccttc accagcgacg 180

tgagcagcta cctggagggc caggccgcca aggagttcat cgcctggctg gtgaagggcc 240

gcggc 245

<210> 18
<211> 77
<212> PRT
<213> Artificial

<220>
<223> Amino acid sequence of Factor IX.GLP-1Gly8

<400> 18

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg His Gly
35 40 45

Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala
50 55 60

Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
65 70 75

<210> 19
<211> 254
<212> DNA

<213> Artificial Sequence

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<223> Nucleotide sequence of Exendin-4 (IGF-1).GLP-1Gly8

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ccagctccga gagccctctg aagcctgcca agtctgccag acatggagag ggcaccttca 180

catctgacgt gagcagctac ctggagggcc aggccgccaa ggagttcatc gcctggctgg 240

tgaagggccg cggc 254

<210> 20
<211> 80
<212> PRT
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<220>
<223> Amino acid sequence of Exendin-4 (IGF-1).GLP-1Gly8

<400> 20

Met Lys Ile Ile Leu Trp Leu Cys Val Phe Gly Leu Phe Leu Ala Thr
1 5 10 15

Leu Phe Pro Ile Ser Trp Gln Met Pro Val Glu Ser Gly Leu Ser Ser
20 25 30

Glu Asp Ser Ala Ser Ser Glu Ser Pro Leu Lys Pro Ala Lys Ser Ala
35 40 45

Arg His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu
50 55 60

Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
65 70 75 80

<210> 21
<211> 31
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<220>
<223> GLP-1(7-37)

<400> 21

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
20 25 30

<210> 22
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; Gly8-GLP-1 (7-37)

<400> 22

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1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
20 25 30

<210> 23
<211> 28
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; GLP-1 (7-34)

<400> 23

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys
20 25

<210> 24
<211> 29
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; GLP-1 (7-35)

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His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
20 25

<210> 25
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; GLP-1 (7-36)

<400> 25

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly

1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
20 25 30

<210> 26
<211> 31
<212> PRT
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<220>
<223> Modified GLP-1 molecule; Val8-GLP-1 (7-37)

<400> 26

His Val Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
20 25 30

<210> 27
<211> 31
<212> PRT
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<220>
<223> Modified GLP-1 molecule; Gln9-GLP-1 (7-37)

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His Ala Gln Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
20 25 30

<210> 28
<211> 31
<212> PRT
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<220>
<223> Modified GLP-1 molecule; Thr16-Lys18-GLP-1 (7-37)

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1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
20 25 30

<210> 29
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<212> PRT
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<220>
<223> Modified GLP-1 molecule; Lys18-GLP-1 (7-37)

<400> 29

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Lys Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
20 25 30

<210> 30
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<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; D-Gln9-GLP-1 (7-37)

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His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
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Gln Ala Ala Lys Glu Phe Ile Gln Trp Leu Val Lys Gly Arg Gly
20 25 30

<210> 31
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<212> PRT
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<220>
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Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val
20 25 30

Lys Gly Arg Gly
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<210> 32
<211> 35
<212> PRT
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<220>
<223> Modified GLP-1 molecule; GLP-1 (3-37)

<400> 32

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1 5 10 15

Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys
20 25 30

Gly Arg Gly
35

<210> 33
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified GLP-1 molecule; GLP-1 (6-37)

<400> 33

Arg His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu
1 5 10 15

Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
20 25 30

<210> 34
<211> 4
<212> PRT
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<220>
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<220>
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<222> (2)..(2)
<223> Xaa can be any naturally occurring amino acid

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<220>
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<223> Xaa can be any naturally occurring amino acid

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<213> Artificial Sequence

<220>
<223> Recognition site for furin cleavage

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<222> (1)..(1)
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<220>
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<222> (3)..(3)
<223> Xaa can be any naturally occurring amino acid

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> Xaa can be either Lys or Arg

<400> 36

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<210> 37
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<220>
<223> Recognition site for furin cleavage

<220>
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<220>
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<400> 38

Arg Gln Lys Arg

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<210> 39
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> IGF-1 signal sequence

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<210> 40
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified IGF-1 signal sequence

<400> 40

Pro Leu Lys Pro Ala Lys Ser Lys Arg
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<210> 41
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified IGF-1 signal sequence

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<210> 42
<211> 9
<212> PRT
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<220>
<223> Modified IGF-1 signal sequence

<400> 42

Pro Leu Arg Pro Ala Lys Ser Ala Arg
1 5

<210> 43
<211> 9
<212> PRT
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<220>

<223> Modified IGF-1 signal sequence

<400> 43

Pro Leu Ala Pro Ala Lys Ser Ala Arg
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<210> 44
<211> 9
<212> PRT
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<220>
<223> Modified IGF-signal 1 sequence

<400> 44

Pro Leu Lys Pro Ala Arg Ser Lys Arg
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<210> 45
<211> 9
<212> PRT
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<220>
<223> Modified IGF-1 signal sequence

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Pro Leu Arg Pro Ala Lys Ser Lys Arg
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<210> 46
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified IGF-1 signal sequence

<400> 46

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<210> 47
<211> 9
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<220>
<223> Modified IGF-1 signal sequence

<400> 47

Pro Leu Ala Pro Ala Lys Ser Lys Arg
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<210> 48

<211> 9
<212> PRT
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<220>
<223> Modified IGF-1 signal sequence

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Pro Leu Ala Pro Ala Arg Ser Lys Arg
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<210> 49
<211> 9
<212> PRT
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<220>
<223> Modified IGF-1 signal sequence

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Pro Leu Ala Pro Ala Arg Ser Ala Arg
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<210> 50
<211> 9
<212> PRT
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<220>
<223> Modified IGF-1 signal sequence

<400> 50

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<210> 51
<211> 33
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<220>
<223> 5705DA

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<210> 52
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<220>
<223> 5706DA

<400> 52
gtcctccact tcacgcttgg agcggggtgt 30

<210> 53
<211> 51
<212> DNA
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<220>
<223> Annealed oligonucleotides containing a polylinker for cloning

<400> 53
gatctcctag gggtttcgaa accactagta agcttaccgc atgccttaag g 51

<210> 54
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Annealed oligonucleotides containing a polylinker for cloning

<400> 54
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